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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/829,661	04/22/2004	Xiang-Yang Han	UTSC:865US	7698

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EXAMINER	
HINES, JANA A	
ART UNIT	PAPER NUMBER
1645	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/21/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/829,661	HAN ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-63* is/are pending in the application.

4a) Of the above claim(s) *16-17, 21, 26-29, 33-40, 50-54 and 58-59* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,18-20,22-25,30-32,41-49,55-57 and 60-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-63* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/6/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicants have elected to prosecute claims 1-63, drawn to SEQ ID NO:1 and the *Aspergillus* species. Claims 16-17, 21, 26-29, 33-40, 50-54 and 58-59 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention. The election was made **without** traverse in the reply filed on January 3, 2007.

2. Claims 1-15, 18-20, 22-25, 30-32, 41-49, 55-57 and 60-63 are under consideration in this office action.

Information Disclosure Statement

3. The information disclosure statement (IDS) submitted on March 16, 2005 was filed. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Specification

4. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Objections

5. Claim 46 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is

required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 46 is drawn to obtaining the sample from the subject, however claim 1 already recited that the sample is obtained from the subject. Therefore the claim does not appear to be further limiting and clarification is required to overcome the objection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 14, 15, 32, 49 and 55-57 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to probes that comprise nucleic acids that hybridizes to fragments thereof; or primers that comprise nucleic acids to the nucleic acid sequence of SEQ ID NO:1 or fragments thereof. The instant specification and claims are encompassing currently unidentified nucleic acid molecules and claiming that these nucleic acids have the capability of hybridizing to SEQ ID NO:1 or fragments thereof. Therefore, there is evidence that claimed nucleic acids have not yet been identified.

Moreover, the instant specification fails to disclose the specific nucleic acid comprised within the probe that hybridize to SEQ ID NO:1. In view of the lack of evidence, it is apparent that Applicants were not in possession of all or many probes that comprise nucleic acids that hybridizes to fragments thereof; or primers that comprise nucleic acids to the nucleic acid sequence of SEQ ID NO:1 or fragments thereof at the time of filing the instant application.

The specification does not place any structure, chemical or absolute functional limitations on the nucleic acid molecule per se. It is noted that the nucleic acid molecule only be capable of hybridizing and not that the molecule actually hybridizes to SEQ ID NO:1. The recitation of a nucleic acid molecule does not convey a common structure or function. The scope of the claims includes numerous structural variants and the genus is highly variant because a significant number of structural differences between the genus members are permitted. The specification fails to provide guidance on the structure of the nucleic acid molecules. Structural features that could distinguish molecules in the genus from others in the class are missing from the disclosure and the claims. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description, because specific, not general guidance is needed.

The nucleic acid molecule comprising one or more nucleic acids is defined by its activity of function, i.e., the capability to hybridizing to a nucleotide sequence of SEQ ID NO:1 or fragments thereof. While the description of the ability of the claimed probe which hybridizes may generically describe the nucleic acid molecule's function, it does

not describe the nucleic acid molecule itself. The hybridization capability distinction is a purely functional distinction. Thus, a description of the nucleic acid molecule by what it does, such as hybridizing to a nucleotide sequence of SEQ ID NO:1 or fragments thereof is insufficient. Since the disclosure fails to describe the common attributes or structural characteristics that identify the members of the genus, and because the genus of nucleic acid molecules of is highly variable, the function of hybridization alone is insufficient to describe the genus of nucleic acid molecules.

An adequate description requires more than a mere statement that it is part of the invention. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ 2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Lts.*, 18 USPQ2d 1016. Encoding distinguishes the claimed nucleotide sequences from unclaimed sequences only by what they do, which is a purely functional distinction. Even where there is an actual reduction to practice, which may demonstrate possession of an embodiment of an invention, it does not necessarily describe what the claimed invention is. The instant claims describe a nucleic acid molecule described by its function i.e., hybridization, however this description does not describe the claimed nucleic acid molecules themselves. See also, *In The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), where the court held that a generic statement that defines a genus of nucleic acids by only their functional activity does not provide an adequate description of the genus. The court indicated that while Applicants are not required to disclose every species encompassed by a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, usually defined by a nucleotide sequence, falling within the scope of the claimed genus. At section B(1), the court states that "An adequate written description of a DNA...'requires

a precise definition, such as by structure, formula, chemical name, or physical properties', not a mere wish or plan for obtaining the claimed chemical invention".

The written description in this case only sets forth specific sequences, therefore the written description is not commensurate in scope with the claims drawn to fragments thereof. Neither the specification nor the claims teach how to define fragments thereof. Neither the claims nor the specification teach how to obtain such fragments. There is no guidance as to what the fragments are; or what fragments can or cannot be used in the nucleic acid molecule being claimed. The specification does not include structural examples fragments thereof. Thus, the resulting fragment could result in a complex not taught and enabled by the specification.

Vas-Cath Inc. V. Mahurkar, 19 USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (*See Vas-Cath* at page 1116).

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision (see page 115).

In view of these considerations, a person skilled in the art would not have viewed the teachings of the specification sufficient to show that applicants were in possession of probes that comprise nucleic acids that hybridizes to fragments thereof; or primers that comprise nucleic acids to the nucleic acid sequence of SEQ ID NO:1 or fragments thereof. Therefore the full breadth of the claims fails to meet the written description provision of 35 USC 112, first paragraph.

7. Claims 4 and 12-13 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a) Claim 4 states that the sample is mixed with "a nucleic acid" that encodes RNA, however it is unclear how a single nucleic acid will encode the 5.8S ribosomal RNA. Therefore, clarification is required to overcome the rejection.

b) Claim 12 recites the limitation "the signal" in the claim. There is insufficient antecedent basis for this limitation in the claim. Furthermore, it is unclear how the signal will be compared when no means for supplying a signal have been claimed. Therefore, clarification is required to overcome the rejection.

c) Claim 13 recites the limitation "the exponential phase" in the claim. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-9, 23-25, 30-32, 41-42, 46-48, 55-56, and 60-63 are rejected under 35 U.S.C. 102(b) as being anticipated by Morrison et al., (WO 98/50584).

The claims are drawn to a method for detecting the presence of a mold infection in a subject comprising identifying 5.8S ribosomal RNA or a DNA encoding the RNA in a

sample obtained from a subject. The dependant claims are drawn to specific types of mold, mixing steps, amplification by PCR, determination steps, isolation step and sample types. The claims are also drawn to a kit comprising hybridizing primers and reagents for an amplification reaction.

Morrison et al., teach nucleic acids for detecting *Aspergillus* species and other filamentous fungi in clinical and laboratory settings. The invention uses isolated from fungal DNA from host samples and applies specific probes for diagnosis wherein these probes can be used for *in situ* hybridization or *in situ* PCR (page 3, lines 25-31). Morrison teaches isolated nucleic acid probes which will selectively hybridize with samples containing nucleic acids from *Aspergillus* (page 5, lines 3-5). The fungi can be detected after PCR reaction or ligase chain reaction amplification of fungal DNA and specific probing of amplified DNA with DNA labeled probes (page 5, lines 7-13). The invention also discloses probes and primers which selectively hybridize to the complementary or opposite, strand of DNA (page 5, lines 36-37). The DNA is preferably amplified using universal primers derived from 5.8S regions of fungal rDNA (page 7, lines 5-8). The primers are comprised of nucleic acids that will hybridize to the sequence of SEQ ID NO:1 or fragments or variants thereof, because both are from the gene of the 5.8S region, thereby allowing for identification of the 5.8S. Detection is achieved by hybridizing the amplified DNA with the specific probe that selectively hybridizes with the DNA (page 7, lines 10-12). Therefore the presence or absence of amplified product is determined. DNA detection of hybridization is indicative of the presence of the particular genus or species of fungus (page 7, lines 12-14).

Morrison et al., teach for the extraction of fungal DNA and PCR amplification teach a PCR assay employing primers for the amplification of both a portion and the entire 5.8S rDNA region, amplicon detection (page 7-8, Example 1). Thus Morrison et al., teach the identification of DNA encoding the RNA of the 5.8S gene. The sample may be derived from blood, saliva, lung fluids, mucosa, tissues and the like (page 7, lines 2-4). Detection of the nucleic acids, probes or primers can be facilitated by the use of detectable moieties, such as biotin, radioactive labels, enzyme labels, and fluorescent labels (15-21). Morrison et al., teach a reduced identification time, wherein such methods are well known in the art (page 24, lines 8-10). The invention also teaches a kit containing one or more probes, which can be used for detection, along with the reagents necessary for hybridizing and detection (page 7, lines 22-27). PCR amplification used a commercially available DNA reagent kit comprising heat-stable DNA polymerase enzymes, buffers, and deoxynucleotides (page 8, lines 33-37).

Accordingly, Morrison et al., teach all the components of the instantly claimed method and kit.

9. Claims 1, 2, 5-9, 23-25, 32, 41-42, 47-49, 55-57 and 60-63 are rejected under 35 U.S.C. 102(b) as being anticipated by Henry et al (2000. J. Clin. Microbio. Vol.38(4): 1510-1515).

The claims are drawn to a method for detecting the presence of a mold infection in a subject comprising identifying 5.8S ribosomal RNA or a DNA encoding the RNA in a sample obtained from a subject. The dependant claims are drawn to specific types of

mold, mixing steps, amplification by PCR, determination steps, and an isolation step. The claims are also drawn to a kit comprising hybridizing primers and reagents for an amplification reaction.

Henry et al., teach the identification of *Aspergillus* species using Internal Transcribed (IT) spacer regions, ITS 1-5.8S-ITS 2. The ITS regions are located between the 18S and 28S genes, where the rRNA gene for 5.8S RNA separates the two ITS regions (page 1510, col.2). The authors teach a standardized method for identification of *Aspergillus* in blind clinical studies (page 1510, col. 2). The cultures for analysis used *Aspergillus flavus, Aspergillus fumigatus, Aspergillus nidulans, Aspergillus niger* and other species (page 1510-11, Materials and Methods). Henry et al., teach DNA extraction reagents, using commercially available DNA extraction reagents (page 1511, col.1). The ITS region primers allowed the amplification of the intervening 5.8S genes and the ITS noncoding regions (page 1511, col.1). Therefore the art teaches the identification of DNA encoding the RNA of the 5.8S gene. PCR amplification was performed with test sample (page 1511, col.1). Therefore, the art teaches method for detecting the presence of a mold infection in a subject comprising identifying 5.8S ribosomal RNA or a DNA encoding the RNA in a sample obtained from a subject. The ITS 1-5.8S-ITS 2 gene complex sequence is from *Aspergillus* and was made available on GenBank, accession number ATCC 36607, AF138288. This sequence has 100% sequence identity to SEQ ID NO:1, thereby meeting the instantly claimed limitations. The PCR amplification techniques teach a PCR assay comprising PCR buffer, magnesium chloride, high-fidelity DNA polymerase, and deoxynucleotides.

The probes and primers, clearly hybridize to the ribosomal RNA and SEQ ID NO:1. It is noted that claims 62-63 do not provide any additional components to the instantly claimed kit. Therefore the limitations drawn to the components of the kit have been meet.

Accordingly, Henry et al., teach all the components of the instantly claimed method and kit.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 10-15 and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morrison et al., (WO 98/50584) in view of Hogan et al., (US Patent 5,827,651).

The claims are drawn to a method for detecting the presence of a mold infection in a subject comprising identifying 5.8S ribosomal RNA or a DNA encoding the RNA in a sample obtained from a subject further comprising RNA samples, quantitating the amplification product, the use of two probes, the hybridization of the probes and labels.

Morrison et al., has been discussed above as using a DNA encoding rRNA. However Morrison et al., do not specifically teach using RNA samples and quantitating the amplification product.

Hogan et al., teach nucleic acid probes and methods for detecting fungi. The inventions described and claimed herein relate to probes and assays based on the use of genetic material such as RNA and relates to the design and construction of nucleic acid probes and hybridization of such probes to genetic material of target non-viral organisms in assays for detection and/or quantitation thereof in test samples of, e.g., sputum, urine, blood and tissue sections, food, soil and water (col. 1, lines 20-28). Hogan et al., describes constructing DNA probes for use in detecting rRNA sequences in an assay for the detection and/or quantitation of any group of non-viral organisms. Some of the probes are used to detect and/or quantify a single species or strain of non-viral organism and other microorganisms instead of just detecting rRNA as being sufficiently similar in particular organisms or groups of organisms or detecting the presence of non-related organisms (col.2 lines 15-21). Hogan et al., teach that rRNA is single stranded and available for hybridization with sufficiently complementary genetic material once its released (col. 2, lines 60-64). Hogan et al., disclose that there are numerous advantages including accuracy, simplicity, economy and speed (col.3, lines 2-5). Hogan et al., teach that quantitation and detection aid in making accurate and specific identification, and the initiation of effective drug treatment (col.12, lines 10-38). Hogan et al., disclose a hybridization assay to determine the presence or amount of rRNa from a particular non-viral organisms (col.2, lines 33-39). The selection of probes includes the 5.8S rRNA wherein this rRNA molecule contains nucleotide sequences which are highly conserved (col. 5, lines 10-19). Such oligonucleotides will serve as the probe in the DNA/rRNA assay hybridization reaction (col.7, lines 63-66). A test sample

is subjected to conditions which release rRNA from any non-viral organisms present, thereby making the rRNA available for hybridization with sufficiently complementary material (col. 2, lines 60-64). Contact between a probe can be labeled and the rRNA target may be subject to conditions which promote hybridization between the two standards (col. 2, lines 64-67). Selected probes may be labeled by any of the many well known methods, wherein useful labels include enzymes, radiolabels, fluorescent molecules, chemiluminescent molecules, and the like (col. 10, lines 57-64). Hogan et al., teach the quantitation of the amplification product, see Examples 3, 4, and 9 on col.17-20, 20-21 and 28-31).

Therefore, it would have been prima facie obvious at the time of applicants invention to modify the method for detecting the presence of a mould as taught by Morrison wherein the modification incorporates the use of RNA samples and quantitating the amplification products as taught by Hogan et al. No more than routine would have been required to modify the method of Morrison et al., when the art already teaches isolation of RNA and DNA techniques using commercially available reagents, along with hybridization, amplification and PCR procedures, and the detection of a wide variety of fungi and moulds to aid in determining an effective course of drug treatment wherein only routine skill is required to use the already present single stranded rRNA that is available for hybridization as taught by Hogan et al. One of ordinary skill in the art would be motivated to modify the method for detecting the presence of a mould as taught by Morrison because Hogan et al., teach the detection and quantitation of single species or strains of specific organisms is accurate, simple, economical and swift.

Moreover, one of ordinary skill in the art would have a reasonable expectation of success since well known commercially available reagents were used to achieve the method of detection which had been routinely observed in the prior art to quantitate, and detect the presence of mould and aid in making rapid, accurate and specific identification of the mould.

11. Claims 10-15 and 18-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Henry et al (2000. J. Clin. Microbio. Vol.38(4): 1510-1515) in view of Hogan et al., (US Patent 5,827,651).

The claims are drawn to a method for detecting the presence of a mold infection in a subject comprising identifying 5.8S ribosomal RNA or a DNA encoding the RNA in a sample obtained from a subject further comprising RNA samples, quantitating the amplification product, the use of two probes, the hybridization of the probes and labels.

Henry et al., has been discussed above as using a DNA encoding rRNA. However Henry et al., do not specifically teach using RNA samples and quantitating the amplification product.

Hogan et al., teach nucleic acid probes and methods for detecting fungi. The inventions described and claimed herein relate to probes and assays based on the use of genetic material such as RNA and relates to the design and construction of nucleic acid probes and hybridization of such probes to genetic material of target non-viral organisms in assays for detection and/or quantitation thereof in test samples of, e.g., sputum, urine, blood and tissue sections, food, soil and water (col. 1, lines 20-28).

Hogan et al., describes constructing DNA probes for use in detecting rRNA sequences in an assay for the detection and/or quantitation of any group of non-viral organisms. Some of the probes are used to detect and/or quantify a single species or strain of non-viral organism and other microorganisms instead of just detecting rRNA as being sufficiently similar in particular organisms or groups of organisms or detecting the presence of non-related organisms (col.2 lines 15-21). Hogan et al., teach that rRNa is single stranded and available for hybridization with sufficiently complementary genetic material once its released (col. 2, lines 60-64). Hogan et al., disclose that there are numerous advantages including accuracy, simplicity, economy and speed (col.3, lines 2-5). Hogan et al., teach that quantitation and detection aid in making accurate and specific identification, and the initiation of effective drug treatment (col.12, lines 10-38). Hogan et al., disclose a hybridization assay to determine the presence or amount of rRNA from a particular non-viral organism (col.2, lines 33-39). The selection of probes includes the 5.8S rRNA wherein this rRNA molecule contains nucleotide sequences which are highly conserved (col. 5, lines 10-19). Such oligonucleotides will serve as the probe in the DNA/rRNA assay hybridization reaction (col.7, lines 63-66). A test sample is subjected to conditions which release rRNA from any non-viral organisms present, thereby making the rRNA available for hybridization with sufficiently complementary material (col. 2, lines 60-64). Contact between a probe can be labeled and the rRNA target may be subject to conditions which promote hybridization between the two standards (col. 2, lines 64-67). Selected probes may be labeled by any of the many well known methods, wherein useful labels include enzymes, radiolabels, fluorescent

molecules, chemiluminescent molecules, and the like (col. 10, lines 57-64). Hogan et al., teach the quantitation of the amplification product, see Examples 3, 4, and 9 on col.17-20, 20-21 and 28-31).

Therefore, it would have been prima facie obvious at the time of applicants invention to modify the method for detecting the presence of a mould as taught by Henry et al., wherein the modification incorporates the use of RNA samples and quantitating the amplification products as taught by Hogan et al. No more than routine would have been required to modify the method of Henry et al., when the art already teaches isolation techniques using commercially available reagents, along with hybridization, amplification and PCR procedures, and the detection of fungi wherein only routine skill is required to use the already present single stranded rRNA that is available for hybridization as taught by Hogan et al. One of ordinary skill in the art would be motivated to modify the method for detecting the presence of a mould as taught by Henry et al., because Hogan et al., teach the detection and quantitation of single species or strains of specific organisms is accurate, simple, economical and swift. Moreover, one of ordinary skill in the art would have a reasonable expectation of success since well known commercially available reagents were used to achieve the method of detection which had been routinely observed in the prior art to quantitate, and detect the presence of mould and aid in making rapid, accurate and specific identification of the mould.

12. Claims 43-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Morrison et al., (WO 98/50584) in view of Higgins et al., [1999. Annals of the New York Academy of sciences 894(1), pages 130-148].

The claims are drawn to a method for detecting the presence of a mold infection in a subject comprising a detection range of 1 femtogram (fg) to 20 nanogram (ng) or 800fg or 100fg to 200 fg of DNA.

Morrison et al., has been discussed above as teaching the use of nucleic acid sequence based amplification and PCR techniques to detect DNA; however Morrison et al., do not specifically teach a detection range of 1 femtogram (fg) to 20 nanogram (ng), 1fg to 800fg or 100fg to 200 fg of DNA.

Higgins et al., teach nucleic acid based detection protocols which are available to detecting pathogens. The techniques involves the use of olignucleotide primers in conjunction with heat stable polymerases to allow repeated cycling of the reaction in order to synthesize large quantities of the desired gene segment (page 133, para.2). These techniques can be used to both improve the detection limit and determine if the organism in question contains the target genes. PCR allows for the ability to amplify DNA from extremely small quantities of starting material, thus PCR offers DNA detection limits in the femtogram or even attogram range (page 133, para. 3). Because it allows the investigator to design primers unique to gene segments of interest, PCR offers a high level of specificity with discrimination possible at the level of individual nucleotides, particularly oligonucelotide probes (page 133, para. 3). Therefore Higgins et al., clearly teach that the well known amplification and PCR techniques would not

only detect DNA in the 1fg to 20 ng, 1fg to 800fg or 100fg to 200 fg range, it would also allow for detection DNA at even lower limits.

Therefore, it would have been prima facie obvious at the time of applicants invention to modify the method for detecting the presence of a mould using amplification and PCR techniques as taught by Morrison wherein the modification incorporates detection ranges at the femtogram and nanogram level as taught by Higgins. No more than routine would have been required to use the method of Morrison et al., when the art already teaches using commercially available reagents, hybridization, amplification and PCR procedures to detect 5.8S DNA, when the art teaches that basic PCR techniques provide for detection limits in the femtogram and nanogram range. One of ordinary skill in the art would be motivated to detect at such levels, because PCR offers a high level of specificity from extremely small amounts of target material, as taught by Higgins et al. Furthermore, Higgins et al., teach the detection of organisms is specific and accurate. Moreover, one of ordinary skill in the art would have a reasonable expectation of success since well known commercially available reagents were used to achieve the method of detection which had been routinely observed in the prior art to detect the presence of DNA in order to make an accurate and specific identification of a specific mould gene.

Prior Art

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Accensi et al., teach PCR methods to differentiate species in *Aspergillus niger* aggregates. Beck (US Patent 5,814,453) teaches detection of fungal pathogens using PCR. Ferrer et al teach the detection and identification of fungal pathogens by PCR and by ITS and 5.8S rDNA typing. Kumeda et al., teach PCR-amplified rDNA ITS to differentiate species of *Aspergillus flavi*.

Conclusion

14. No claims allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Jeffery Siew, can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines
March 14, 2007

MARK NAVARRO
PRIMARY EXAMINER